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     (FILE 'HOME' ENTERED AT 14:03:26 ON 31 OCT 2007)

     FILE 'REGISTRY' ENTERED AT 14:03:42 ON 31 OCT 2007
L1             STRUCTURE UPLOADED
L2           0 S L1 SAM
L3           0 S L1 SSS SAM
L4          42 S L1 FULL

     FILE 'CAPLUS, USPATFULL, USPATOLD, USPAT2' ENTERED AT 14:12:33 ON 31 OCT
     2007
L5          25 S L4
L6           5 S L5 AND (INFLAMMATION OR CANCER OR TUMOR)
L7          20 S L5 NOT L6

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L8           2 S L4/THU
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     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS'
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L9          42 S L1 FULL

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     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS' ENTERED AT
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L10          0 S E1-E61
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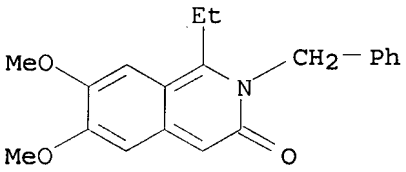
L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41337 CAPLUS
DOCUMENT NUMBER: 140:105253
TITLE: Compounds and methods for treating cancer and inflammation
INVENTOR(S): Zhang, Zaihui; Charest, David L.; Yan, Jun
PATENT ASSIGNEE(S): Kinetek Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004004834	A1	20040115	WO 2003-CA975		20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2491614	A1	20040115	CA 2003-2491614		20030625
AU 2003281245	A1	20040123	AU 2003-281245		20030625
US 2006148848	A1	20060706	US 2005-520250		20051028
PRIORITY APPLN. INFO.:			US 2002-393700P	P	20020702
			WO 2003-CA975	W	20030625

OTHER SOURCE(S): MARPAT 140:105253
TI Compounds and methods for treating cancer and inflammation
AB Methods of using isoquinolone derivs. to treat cancer or inflammation in a mammal and pharmaceutical compns. containing such derivs. are disclosed.
ST antitumor SGK kinase inhibitor cancer inflammation therapy
IT Angiogenesis
Anti-inflammatory agents
Antitumor agents
Apoptosis
Human
Inflammation
Mammalia
Neoplasm
(compds. for treating cancer and inflammation)
IT Interleukin 6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compds. for treating cancer and inflammation)
IT Cell division
(reduction; compds. for treating cancer and inflammation)
IT 178037-70-2, Serum and glucocorticoid inducible kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2α; compds. for treating cancer and

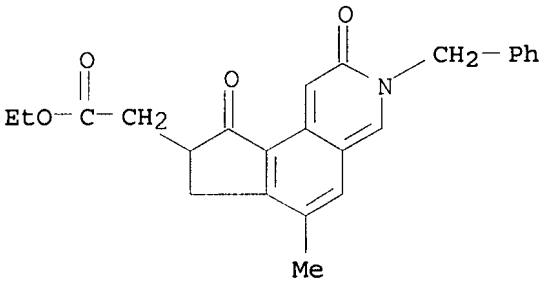
inflammation)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compds. for treating cancer and inflammation)
IT 23214-92-8, Doxorubicin 309720-09-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for treating cancer and inflammation)
IT 309720-09-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for treating cancer and inflammation)
RN 309720-09-0 CAPLUS
CN 3(2H)-Isoquinolinone, 1-ethyl-6,7-dimethoxy-2-(phenylmethyl)- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:331253 CAPLUS
DOCUMENT NUMBER: 129:67683
TITLE: DNA-interacting agents in cancer chemotherapy and cyclopenta[f]isoquinoline derivatives
AUTHOR(S): Kundu, Nitya G.; Nandi, Bidisha; Chang, Jih; Boehme, Phillip H.
CORPORATE SOURCE: Department of Organic Chemistry, Indian Association for the Cultivation of Science, Calcutta, 700 032, India
SOURCE: Journal of the Indian Chemical Society (1997), 74(11-12), 877-883
CODEN: JICSAH; ISSN: 0019-4522
PUBLISHER: Indian Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
TI DNA-interacting agents in cancer chemotherapy and cyclopenta[f]isoquinoline derivatives
AB Cancer chemotherapeutic agents have been briefly reviewed with an emphasis on DNA-binders. The synthesis of a few new cyclopenta[f]isoquinolines is also. . .
IT Antitumor agents
(DNA-interacting agents in cancer chemotherapy)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(DNA-interacting agents in cancer chemotherapy)
IT 55329-88-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-interacting agents in cancer chemotherapy)

IT 209126-27-2P 209126-28-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of cyclopenta[f]isoquinoline derivs.)
IT 209126-27-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of cyclopenta[f]isoquinoline derivs.)
RN 209126-27-2 CAPLUS
CN 2H-Cyclopent[f]isoquinoline-8-acetic acid, 3,7,8,9-tetrahydro-6-methyl-2,9-dioxo-3-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2006:175398 USPATFULL
TITLE: Compounds and methods for treating cancer and inflammation
INVENTOR(S): Zhang, Zaihui, Vancouver, CANADA
Charest, David L, Vancouver, CANADA
Yan, Jun, Coquitlam, CANADA
PATENT ASSIGNEE(S): QLT, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006148848	A1	20060706	
APPLICATION INFO.:	US 2003-520250	A1	20030625	(10)
	WO 2003-CA975		20030625	
			20051028	PCT 371 date

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-393700P	20020702 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092, US
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
LINE COUNT: 1843
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Compounds and methods for treating cancer and inflammation

AB Methods of using isoquinolone derivatives to treat cancer or inflammation in a mammal and pharmaceutical compositions containing such derivatives are disclosed.

SUMM Uncontrolled signaling has been implicated in a variety of disease conditions including, inflammation, cancer, arteriosclerosis, and psoriasis. For example, many cancer causing genes (oncogenes) are protein kinases, enzymes that catalyze protein phosphorylation reactions, or are specifically regulated by phosphorylation. In addition,. . .

SUMM PCT Published Patent Application, WO 02/24947 (Kinetek Pharmaceuticals) describes cancer associated protein kinases and their uses.

SUMM This invention is directed to the use of certain isoquinolone derivatives in treating hyperproliferative disorders, e.g., cancer, inflammation, etc. in a mammal. Of particular interest are hyperproliferative disorders associated with cellular modulation of protein phosphorylation states, i.e. altered. . . are used to inhibit the activity of SGK enzymes. Accordingly, in one aspect, this invention provides a method of treating cancer in a mammal, which method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound. . .

SUMM In another aspect, this invention provides a pharmaceutical composition useful in treating cancer or inflammation in a human, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier, diluent or excipient and a compound of formula. . .

SUMM In another aspect of the invention, the use of the compounds of formula (I) for the treatment of cancer, inflammation, or disorders or condition associated with hyperproliferation and tissue remodelling or repair is provided.

DETD . . . formula (I) which, when administered to a mammal, preferably a human, is sufficient to effect treatment, as defined below, for cancer, inflammation, or neurological disease. The amount of a compound of formula (I) which constitutes a "therapeutically effective amount" will vary depending. . .

DETD (i) preventing cancer or inflammation from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been. . .

DETD (ii) inhibiting cancer or inflammation, i.e., arresting its development; or

DETD (iii) relieving cancer or inflammation, i.e., causing regression of the condition.

DETD . . . of SGK are elevated 2-3 fold in liver and lung tumour tissue compared to control tissue. Immunohistochemical analysis of colon cancer shows elevation of SGK2 in the cytoplasm and SGK2 RNA expression levels are elevated in colon (LS-180 and HT-29) and prostate (LnCaP, DU-145) cancer cell lines as well as a NSCLC cell line (A549). In contrast, expression levels of SGK2 in "normal" cell lines. . .

DETD The compounds and pharmaceutical compositions of the invention are administered to a subject having a cancer or a pathological inflammation in order to inhibit tumour growth by impeding cell division, and to decrease inflammation by inhibiting cell adhesion and cell migration.

DETD . . . regrowth of tumours, prevent metastatic growth, diminish restenosis associated with cardiovascular surgery, to prevent or reduce cell migration leading to inflammation and associated tissue damage. Alternatively, the compounds and pharmaceutical compositions of the invention may be administered to a subject in. . .

DETD Hyperproliferative cell disorders include cancers; blood

vessel proliferative disorders such as restenosis, atherosclerosis, in-stent stenosis, vascular graft restenosis, etc.; fibrotic disorders; inflammatory disorders, e.g. arthritis, etc.; endometriosis; benign growth disorders such as prostate enlargement and lipomas; and autoimmune disorders. Cancers of particular interest include carcinomas, e.g. colon, prostate, breast, melanoma, ductal, endometrial, stomach, dysplastic oral mucosa, invasive oral cancer, non-small cell lung carcinoma, transitional and squamous cell urinary carcinoma, etc.; neurological malignancies, e.g. neuroblastoma, gliomas, etc.; hematological malignancies, e.g.. . .

DETD . . . invention. Other disorders and conditions of interest relate to epidermal hyperproliferation, tissue remodelling and repair. For example, the chronic skin inflammation of psoriasis is associated with hyperplastic epidermal keratinocytes.

DETD . . . in need of such treatment. The compounds and pharmaceutical compositions of the invention are administered to a subject having a cancer or a pathological inflammation in order to inhibit tumour growth by impeding cell division, and to decrease inflammation by inhibiting cell adhesion and cell migration. The compounds of formula (I) may also find use as affinity reagents for. .

DETD . . . the pharmaceutical composition of the present invention may contain one or more known pharmacological agents used in the treatment of cancer or inflammation in a mammal, particularly, cancer or inflammation associated with hyperproliferation and tissue remodelling or repair.

DETD Of the various methods of treating cancer or inflammation in a mammal as set forth above in the Summary of the Invention, a preferred method is that method wherein the cancer or inflammation is associated with hyperproliferation or cell survival. Another preferred method is that method wherein the cancer or inflammation is associated with the activity SGK.

DETD . . . the Summary of the Invention, may not possess pharmacological activity as such, they may be administered to a mammal with cancer or inflammation and thereafter metabolized in the body to form compounds of the invention which are pharmacologically active. Such derivatives may therefore. . .

DETD . . . the proliferation of various tumour cells could be used as an indication of its ability to prevent disease progression in cancer.

DETD A. Establishment of inflammation assay panel.

CLM What is claimed is:

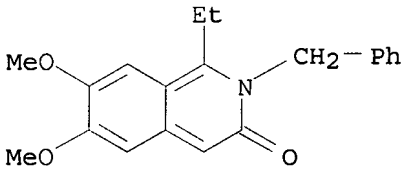
1. A pharmaceutical composition useful in treating cancer, inflammation or a hyperproliferative disorder in a human, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier, diluent or excipient and. . .

40. A method of treating cancer, inflammation or a hyperproliferative disorder in a mammal, which method comprises administering to the mammal in need thereof a therapeutically effective. . .

42. The method according to claim 40 wherein the cancer or inflammation is associated with hyperproliferation or cell survival.

43. The method according to claim 40 wherein the hyperproliferative disease, cancer or inflammation is associated with the activity of SGK.

IT 23214-92-8, Doxorubicin 309720-09-0
(compds. for treating cancer and inflammation)
IT 309720-09-0
(compds. for treating cancer and inflammation)
RN 309720-09-0 USPATFULL
CN 3(2H)-Isoquinolinone, 1-ethyl-6,7-dimethoxy-2-(phenylmethyl)- (CA INDEX NAME)



L6 ANSWER 4 OF 5 USPATFULL on STN
ACCESSION NUMBER: 2004:51528 USPATFULL
TITLE: 3-Isoquinolinone derivatives as matrix metalloproteinase inhibitors
INVENTOR(S): Bunker, Amy Mae, Ann Arbor, MI, UNITED STATES
Sliskovic, Drago Robert, Saline, MI, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004038959	A1	20040226	
	US 6974822	B2	20051213	
APPLICATION INFO.:	US 2003-634180	A1	20030805	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-403062P	20020813 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WARNER-LAMBERT COMPANY, 2800 PLYMOUTH RD, ANN ARBOR, MI, 48105
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 4035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . multiple sclerosis, gingivitis, corneal epidermal and gastric ulceration, atherosclerosis, neointimal proliferation which leads to restenosis and ischemic heart failure, and tumor metastasis. A method for preventing and treating these and other diseases is now recognized to be by inhibiting matrix metalloproteinase. . .
SUMM . . . peptides. Peptide hydroxamates and the natural endogenous inhibitors of MMPs (TIMPs) have been used successfully to treat animal models of cancer and inflammation. MMP inhibitors have also been used to prevent and treat congestive heart failure and other cardiovascular diseases, U.S. Pat. No.. . .
SUMM [0490] 91. A method for treating a cancer, comprising administering to a patient suffering from a cancer a nontoxic anti-cancer effective amount of a compound of Formula I according to Embodiment 1, or a pharmaceutically acceptable salt thereof.
SUMM [0496] 97. A method for treating inflammation, comprising administering to a patient suffering from inflammation a

nontoxic effective amount of a compound of Formula I according to Embodiment 1, or a pharmaceutically acceptable salt thereof.

SUMM . . . compound, or a pharmaceutically acceptable salt thereof, or a tautomer thereof, sufficient to inhibit, halt, or cause regression of the cancer being treated in a particular patient or patient population. For example in humans or other mammals, an anticancer effective amount. . . amount required by the guidelines of the United States Food and Drug Administration, or equivalent foreign agency, for the particular cancer and patient being treated.

SUMM . . . Polyposis-familial adenomatus. Celecoxib is marketed under the tradename "Celebrex". Celecoxib is currently in clinical trials for the treatment of bladder cancer, chemopreventative-lung cancer, and post-operative pain, and is registered for the treatment of dysmenorrhea. Celecoxib has the structure drawn below: ##STR15##

SUMM . . . invention compound in any number of well known assays for measuring determining the invention compound's effects on cartilage damage, arthritis, inflammation, or pain. These assays include in vitro assays that utilize cartilage samples and in vivo assays in whole animals that measure cartilage degradation, inhibition of inflammation, or pain alleviation.

SUMM . . . invention compounds having anti-inflammatory properties may be identified using any one of a number of in vivo animal models of inflammation. For example, for an example of inflammation models, see U.S. Pat. No. 6, 329,429, which is incorporated herein by reference.

SUMM . . . respiratory distress syndrome, asthma, bronchitis, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer (such as solid tumor cancer including colon cancer, breast cancer , lung cancer and prostrate cancer; hematopoietic malignancies including leukemias and lymphomas; Hodgkin's disease; aplastic anemia, skin cancer and familiar adenomatous polyposis), tissue ulceration, peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis, recurrent gastrointestinal lesion, gastrointestinal bleeding, coagulation,. . . and dermatitis), myasthenia gravis, polymyositis, myositis, bursitis, burns, diabetes (including types I and II diabetes, diabetic retinopathy, neuropathy and nephropathy), tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, immunodeficiency diseases (such as AIDS in humans and FLV, FIV in cats), sepsis, premature labor, hypoprothrombinemia,. . .

SUMM . . . least one other matrix metalloproteinase enzyme such as, for example, MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, or MMP-14, or versus tumor necrosis factor alpha convertase ("TACE"). A preferred aspect of the present invention is novel compounds that are selective inhibitors of. . .

SUMM [0713] B.) where a multi-fold treatment of pain and inflammation is desired, said inhibitory compound is administered in combination with inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting essentially of:

SUMM [0751] The active ingredient of the present invention may be administered in combination with inhibitors of other mediators of inflammation, comprising one or more members selected from the group consisting essentially of the classes of such inhibitors and examples thereof. . .

SUMM . . . The invention compounds may be used in combination with

biological therapeutics useful for treating arthritic conditions, including CP-870, etanercept (a tumor necrosis factor alpha ("TNF-alpha") receptor immunoglobulin molecule; trade names ENBREL® and ENBREL ENTANERCEPT® by Immunex Corporation, Seattle, Wash.), infliximab (an. . .

SUMM . . . which are invention compounds, and pharmaceutically acceptable salts thereof, are thus therapeutically superior to other inhibitors of MMP-13, or even tumor necrosis factor-alpha converting enzyme ("TACE"), because of fewer undesirable side effects from inhibition of the other MMP enzymes or TACE.. . .

SUMM . . . advantage is that the disease modifying properties of the invention compounds provide patients suffering from cartilage damage, arthritis, preferably osteoarthritis, inflammation and/or pain with both relief of symptoms and prevention or inhibition of the underlying disease pathology such as cartilage degradation.. . .

DETD . . . expected from the analysis of proteoglycan loss would establish that an invention compound is effective for inhibiting cartilage damage and inflammation and/or alleviating pain in mammalian patients, including human.

DETD [0942] Another animal model for measuring effects of an invention compound on cartilage damage and inflammation and/or pain is described below in Biological Method 6.

DETD [0953] The foregoing studies would establish that an invention compound is effective for the inhibition of cartilage damage and inflammation and/or alleviating pain, and thus useful for the treatment of osteoarthritis or rheumatoid arthritis in human, and other mammalian disorders. Such a treatment offers a distinct advantage over existing treatments that only modify pain or inflammation or and other secondary symptoms. The effectiveness of an invention compound in this model would indicate that the invention compound will have clinically useful effects in preventing and/or treating cartilage damage, pain and/or inflammation.

DETD . . . administration of a COX-2 inhibitor in accordance with the invention combination may be carried out as described above to treat inflammation, arthritic pain, pain associated with menstrual cramping, and migraines, while an invention compound may be administered to treat OA or. . .

IT 662139-31-3P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-27-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-28-8P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-29-9P, 7-(3-Phenylprop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-30-2P, 2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one 662139-32-4P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-33-5P, 2-(3-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-34-6P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzonitrile 662139-35-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzenesulfonamide 662139-36-8P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-37-9P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-38-0P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-39-1P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-

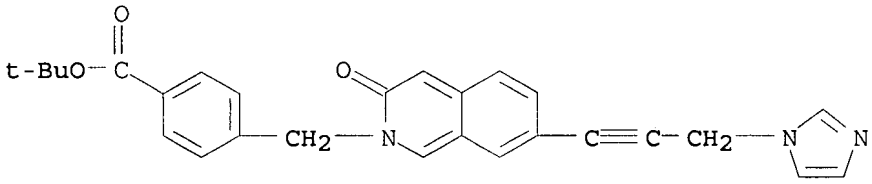
isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-40-4P, 2-(4-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-41-5P, 7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-42-6P, 2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-43-7P, 2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-44-8P, 4-[[3-Oxo-7-[3-([1,2,4]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-45-9P, 4-[(7-Bromo-3-oxo-2H-isoquinolin-2-yl)methyl]benzoic acid tert-butyl ester
(intermediate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-31-3P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

RN 662139-31-3 USPATFULL

CN Benzoic acid, 4-[[7-[3-(1H-imidazol-1-yl)-1-propynyl]-3-oxo-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

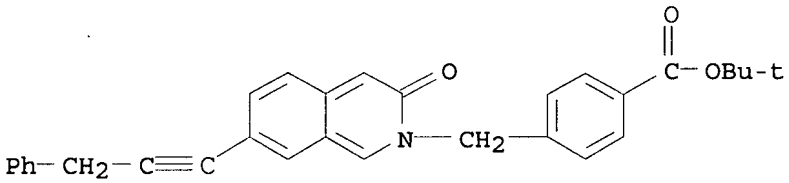


IT 662139-27-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-28-8P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-29-9P, 7-(3-Phenylprop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-30-2P, 2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one 662139-32-4P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-33-5P, 2-(3-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-34-6P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzonitrile 662139-35-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzenesulfonamide 662139-36-8P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-37-9P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-38-0P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-39-1P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-40-4P, 2-(4-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-41-5P, 7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-42-6P, 2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-43-7P, 2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-44-8P, 4-[[3-Oxo-7-[3-([1,2,4]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13

inhibitors for use as antiarthritics)

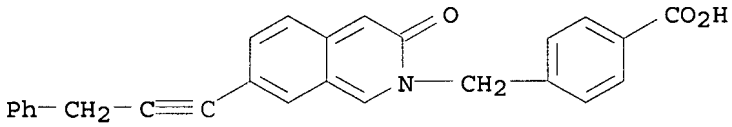
RN 662139-27-7 USPATFULL

CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



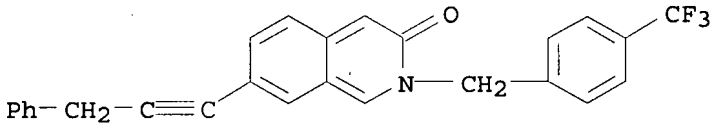
RN 662139-28-8 USPATFULL

CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



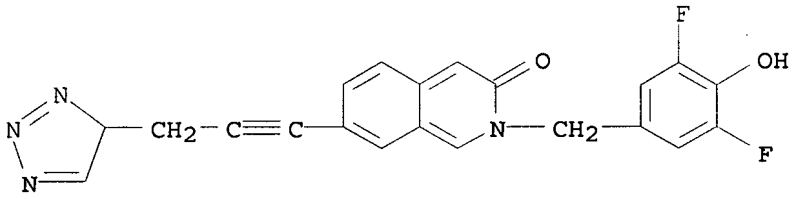
RN 662139-29-9 USPATFULL

CN 3(2H)-Isoquinolinone, 7-(3-phenyl-1-propynyl)-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



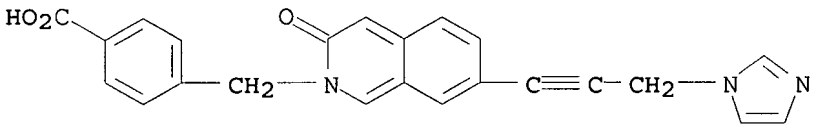
RN 662139-30-2 USPATFULL

CN 3(2H)-Isoquinolinone, 2-[(3,5-difluoro-4-hydroxyphenyl)methyl]-7-[3-(4H-1,2,3-triazol-4-yl)-1-propynyl]- (9CI) (CA INDEX NAME)

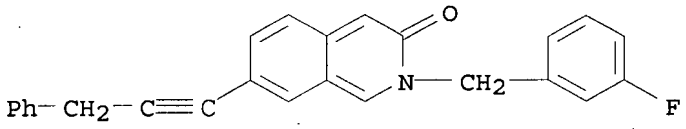


RN 662139-32-4 USPATFULL

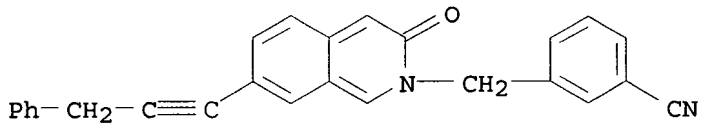
CN Benzoic acid, 4-[[7-[3-(1H-imidazol-1-yl)-1-propynyl]-3-oxo-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



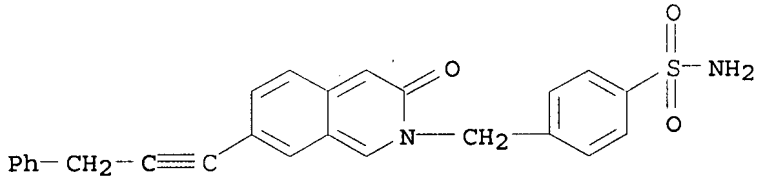
RN 662139-33-5 USPATFULL
CN 3(2H)-Isoquinolinone, 2-[(3-fluorophenyl)methyl]-7-(3-phenyl-1-propynyl)-(9CI) (CA INDEX NAME)



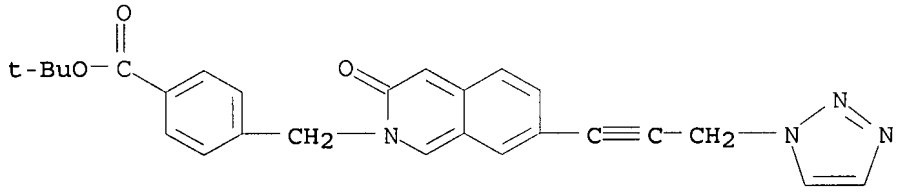
RN 662139-34-6 USPATFULL
CN Benzonitrile, 3-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



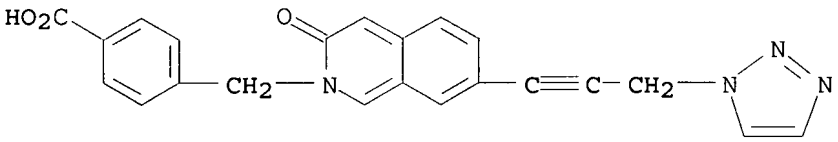
RN 662139-35-7 USPATFULL
CN Benzenesulfonamide, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



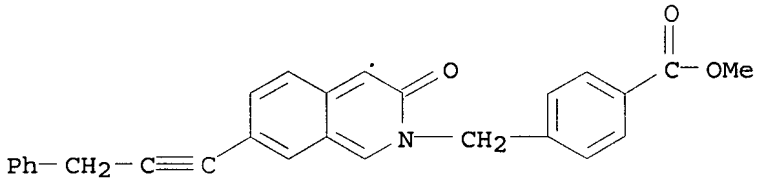
RN 662139-36-8 USPATFULL
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,3-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



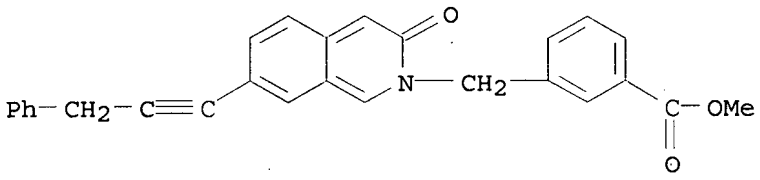
RN 662139-37-9 USPATFULL
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,3-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



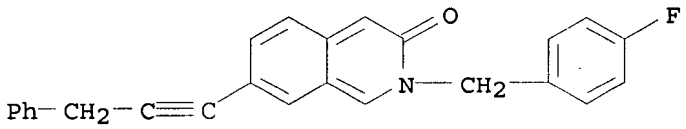
RN 662139-38-0 USPATFULL
CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



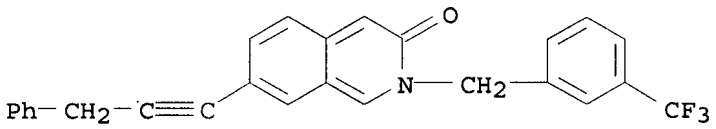
RN 662139-39-1 USPATFULL
CN Benzoic acid, 3-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



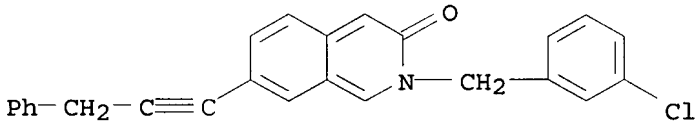
RN 662139-40-4 USPATFULL
CN 3(2H)-Isoquinolinone, 2-[(4-fluorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



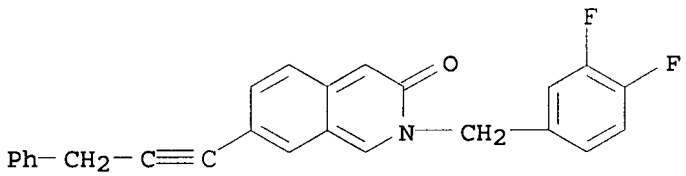
RN 662139-41-5 USPATFULL
CN 3(2H)-Isoquinolinone, 7-(3-phenyl-1-propynyl)-2-[[3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



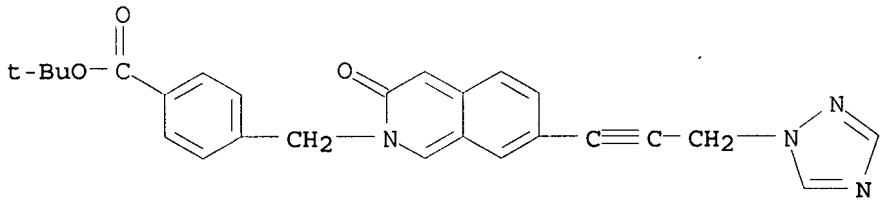
RN 662139-42-6 USPATFULL
CN 3(2H)-Isoquinolinone, 2-[(3-chlorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



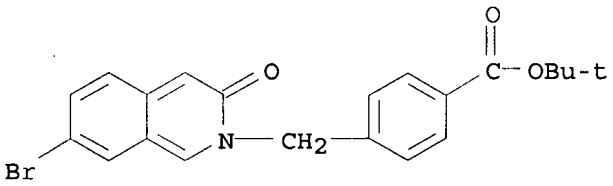
RN 662139-43-7 USPATFULL
CN 3(2H)-Isoquinolinone, 2-[(3,4-difluorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



RN 662139-44-8 USPATFULL
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,4-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 662139-45-9P, 4-[(7-Bromo-3-oxo-2H-isoquinolin-2-yl)methyl]benzoic acid tert-butyl ester
(intermediate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)
RN 662139-45-9 USPATFULL
CN Benzoic acid, 4-[(7-bromo-3-oxo-2(3H)-isoquinolinyl)methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



L6 ANSWER 5 OF 5 USPAT2 on STN

ACCESSION NUMBER:	2004:51528 USPAT2
TITLE:	3-isoquinolinone derivatives as matrix metalloproteinase inhibitors
INVENTOR(S):	Bunker, Amy Mae, Ann Arbor, MI, UNITED STATES Sliskovic, Drago Robert, Saline, MI, UNITED STATES
PATENT ASSIGNEE(S):	Warner-Lambert Company LLC, Morris Plains, NJ, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6974822	B2	20051213	
APPLICATION INFO.:	US 2003-634180		20030805	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2002-403062P	20020813	(60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Rao, Deepak
LEGAL REPRESENTATIVE:	Pfizer Inc., Ashbrook, Charles W., Purchase, Jr., Claude F.
NUMBER OF CLAIMS:	10
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	0 Drawing Figure(s); 0 Drawing Page(s)
LINE COUNT:	3735

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . multiple sclerosis, gingivitis, corneal epidermal and gastric ulceration, atherosclerosis, neointimal proliferation which leads to restenosis and ischemic heart failure, and tumor metastasis. A method for preventing and treating these and other diseases is now recognized to be by inhibiting matrix metalloproteinase. . .

SUMM . . . peptides. Peptide hydroxamates and the natural endogenous inhibitors of MMPs (TIMPs) have been used successfully to treat animal models of cancer and inflammation. MMP inhibitors have also been used to prevent and treat congestive heart failure and other cardiovascular diseases, U.S. Pat. No.. . .

SUMM . . . according to any one of Embodiments 2 to 76, or a pharmaceutically acceptable salt thereof.

91. A method for treating a cancer, comprising administering to a patient suffering from a cancer a nontoxic anti-cancer effective amount of a compound of Formula I according to Embodiment 1, or a pharmaceutically acceptable salt thereof.

92. The method. . . is according to any one of Embodiments 2 to 76, or a pharmaceutically acceptable salt thereof.

97. A method for treating inflammation, comprising administering to a patient suffering from inflammation a nontoxic effective amount of a compound of Formula I according to Embodiment 1, or a pharmaceutically acceptable salt thereof.

98. . .

DETD . . . compound, or a pharmaceutically acceptable salt thereof, or a tautomer thereof, sufficient to inhibit, halt, or cause regression of the cancer being treated in a particular patient or patient population. For example in humans or other mammals, an anticancer effective amount. . . amount required by the guidelines of the United States Food and Drug Administration, or equivalent foreign agency, for the particular cancer and patient being treated.

DETD . . . Polyposis-familial adenomatus. Celecoxib is marketed under the tradename "Celebrex". Celecoxib is currently in clinical trials for the treatment of bladder cancer, chemopreventative-lung cancer, and post-operative pain, and is registered for the treatment of dysmenorrhea. Celecoxib has the structure drawn below: ##STR15##

DETD . . . invention compound in any number of well known assays for measuring determining the invention compound's effects on cartilage damage, arthritis, inflammation, or pain. These assays include in vitro assays that utilize cartilage samples and in vivo assays in whole animals that measure cartilage degradation, inhibition of inflammation, or pain alleviation.

DETD . . . invention compounds having anti-inflammatory properties may be identified using any one of a number of in vivo animal models of inflammation. For example, for an example of inflammation models, see U.S. Pat. No. 6,329,429, which is incorporated herein by reference.

DETD . . . respiratory distress syndrome, asthma, bronchitis, chronic obstructive pulmonary disease, Alzheimer's disease, organ transplant toxicity, cachexia, allergic reactions, allergic contact hypersensitivity, cancer (such as solid tumor cancer including colon cancer, breast cancer , lung cancer and prostrate cancer; hematopoietic malignancies including leukemias and lymphomas; Hodgkin's disease; aplastic anemia, skin cancer and familiar adenomatous polyposis), tissue ulceration, peptic ulcers, gastritis, regional enteritis, ulcerative colitis, diverticulitis, recurrent gastrointestinal lesion, gastrointestinal bleeding, coagulation,. . . and dermatitis), myasthenia gravis, polymyositis, myositis, bursitis, burns, diabetes (including types I and II diabetes, diabetic retinopathy, neuropathy and nephropathy), tumor invasion, tumor growth, tumor metastasis, corneal scarring, scleritis, immunodeficiency diseases (such as AIDS in humans and FLV, FIV in cats), sepsis, premature labor, hypoprothrombinemia,. . .

DETD . . . least one other matrix metalloproteinase enzyme such as, for example, MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, or MMP-14, or versus tumor necrosis factor alpha convertase ("TACE"). A preferred aspect of the present invention is novel compounds that are selective inhibitors of. . .

DETD B.) where a multi-fold treatment of pain and inflammation is desired, said inhibitory compound is administered in combination with inhibitors of other mediators of inflammation, comprising one or more members independently selected from the group consisting essentially of:

DETD The active ingredient of the present invention may be administered in combination with inhibitors of other mediators of inflammation , comprising one or more members selected from the group consisting essentially of the classes of such inhibitors and examples thereof. .

DETD The invention compounds may be used in combination with biological therapeutics useful for treating arthritic conditions, including CP-870,

etanercept (a tumor necrosis factor alpha ("TNF-alpha") receptor immunoglobulin molecule; trade names ENBREL® and ENBREL ENTANERCEPT® by Immunex Corporation, Seattle, Wash.), infliximab (an. . .

DETD . . . which are invention compounds, and pharmaceutically acceptable salts thereof, are thus therapeutically superior to other inhibitors of MMP-13, or even tumor necrosis factor-alpha converting enzyme ("TACE"), because of fewer undesirable side effects from inhibition of the other MMP enzymes or TACE.. . .

DETD . . . advantage is that the disease modifying properties of the invention compounds provide patients suffering from cartilage damage, arthritis, preferably osteoarthritis, inflammation and/or pain with both relief of symptoms and prevention or inhibition of the underlying disease pathology such as cartilage degradation.. . .

DETD . . . expected from the analysis of proteoglycan loss would establish that an invention compound is effective for inhibiting cartilage damage and inflammation and/or alleviating pain in mammalian patients, including human.

DETD Another animal model for measuring effects of an invention compound on cartilage damage and inflammation and/or pain is described below in Biological Method 6.

DETD The foregoing studies would establish that an invention compound is effective for the inhibition of cartilage damage and inflammation and/or alleviating pain, and thus useful for the treatment of osteoarthritis or rheumatoid arthritis in human, and other mammalian disorders. Such a treatment offers a distinct advantage over existing treatments that only modify pain or inflammation or and other secondary symptoms. The effectiveness of an invention compound in this model would indicate that the invention compound will have clinically useful effects in preventing and/or treating cartilage damage, pain and/or inflammation.

DETD . . . administration of a COX-2 inhibitor in accordance with the invention combination may be carried out as described above to treat inflammation, arthritic pain, pain associated with menstrual cramping, and migraines, while an invention compound may be administered to treat OA or. . .

IT 662139-31-3P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-27-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-28-8P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-29-9P, 7-(3-Phenylprop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-30-2P, 2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one 662139-32-4P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-33-5P, 2-(3-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-34-6P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzonitrile 662139-35-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzenesulfonamide 662139-36-8P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-37-9P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-38-0P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-39-1P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-40-4P,

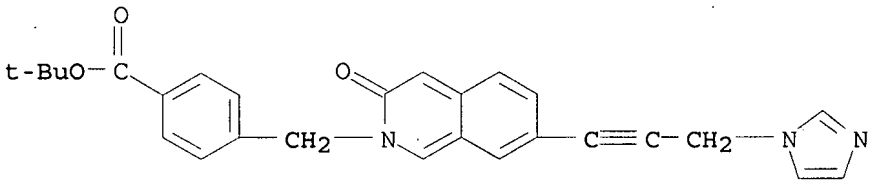
2-(4-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-41-5P, 7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-42-6P, 2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-43-7P, 2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-44-8P, 4-[[3-Oxo-7-[3-([1,2,4]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-45-9P, 4-[(7-Bromo-3-oxo-2H-isoquinolin-2-yl)methyl]benzoic acid tert-butyl ester
(intermediate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

IT 662139-31-3P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

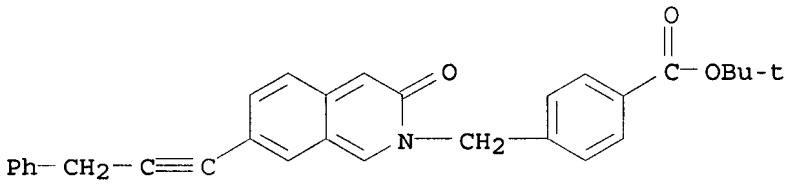
RN 662139-31-3 USPAT2

CN Benzoic acid, 4-[[7-[3-(1H-imidazol-1-yl)-1-propynyl]-3-oxo-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

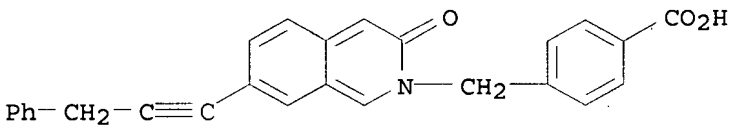


IT 662139-27-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-28-8P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-29-9P, 7-(3-Phenylprop-1-ynyl)-2-(4-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-30-2P, 2-(3,5-Difluoro-4-hydroxybenzyl)-7-[3-(4H-[1,2,3]triazol-4-yl)prop-1-ynyl]-2H-isoquinolin-3-one 662139-32-4P, 4-[[7-[3-(Imidazol-1-yl)prop-1-ynyl]-3-oxo-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-33-5P, 2-(3-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-34-6P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzonitrile 662139-35-7P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzenesulfonamide 662139-36-8P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester 662139-37-9P, 4-[[3-Oxo-7-[3-([1,2,3]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid 662139-38-0P, 4-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-39-1P, 3-[[3-Oxo-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-2-yl]methyl]benzoic acid methyl ester 662139-40-4P, 2-(4-Fluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-41-5P, 7-(3-Phenylprop-1-ynyl)-2-(3-trifluoromethylbenzyl)-2H-isoquinolin-3-one 662139-42-6P, 2-(3-Chlorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-43-7P, 2-(3,4-Difluorobenzyl)-7-(3-phenylprop-1-ynyl)-2H-isoquinolin-3-one 662139-44-8P, 4-[[3-Oxo-7-[3-([1,2,4]triazol-1-yl)prop-1-ynyl]-2H-isoquinolin-2-yl]methyl]benzoic acid tert-butyl ester
(drug candidate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)

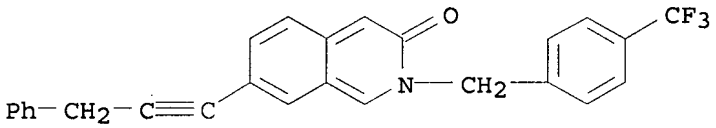
RN 662139-27-7 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



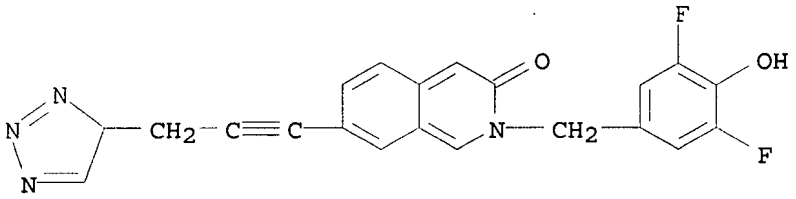
RN 662139-28-8 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



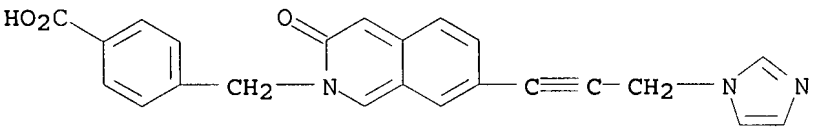
RN 662139-29-9 USPAT2
CN 3(2H)-Isoquinolinone, 7-(3-phenyl-1-propynyl)-2-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



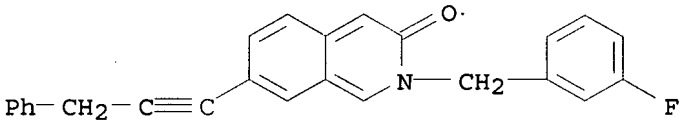
RN 662139-30-2 USPAT2
CN 3(2H)-Isoquinolinone, 2-[(3,5-difluoro-4-hydroxyphenyl)methyl]-7-[3-(4H-1,2,3-triazol-4-yl)-1-propynyl]- (9CI) (CA INDEX NAME)



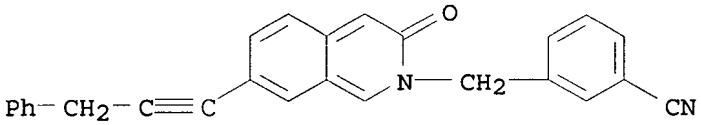
RN 662139-32-4 USPAT2
CN Benzoic acid, 4-[[7-[3-(1H-imidazol-1-yl)-1-propynyl]-3-oxo-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



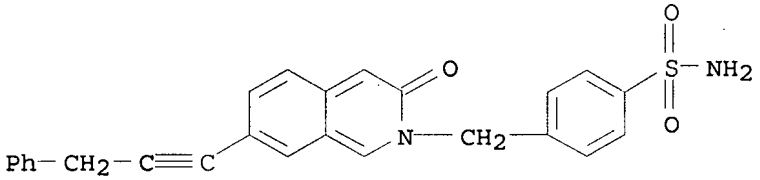
RN 662139-33-5 USPAT2
CN 3(2H)-Isoquinolinone, 2-[(3-fluorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



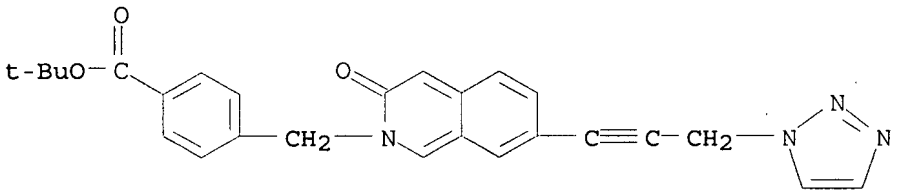
RN 662139-34-6 USPAT2
CN Benzonitrile, 3-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



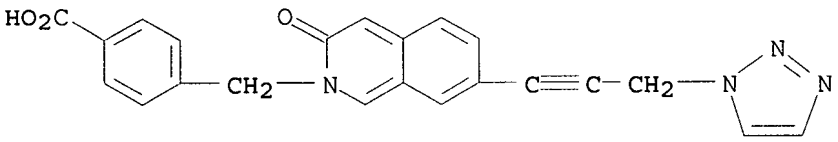
RN 662139-35-7 USPAT2
CN Benzenesulfonamide, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



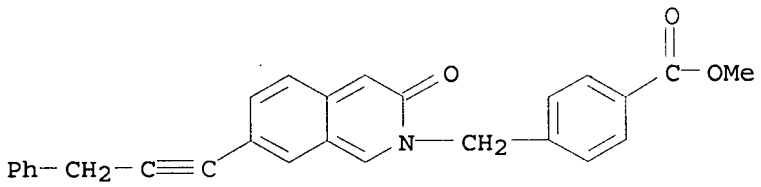
RN 662139-36-8 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,3-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



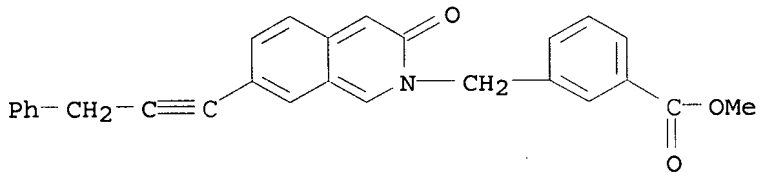
RN 662139-37-9 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,3-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]- (9CI) (CA INDEX NAME)



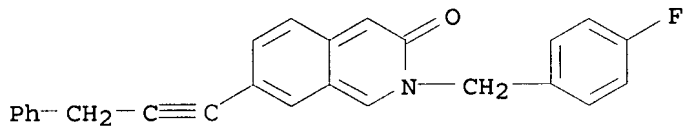
RN 662139-38-0 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



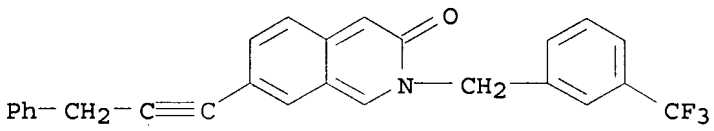
RN 662139-39-1 USPAT2
CN Benzoic acid, 3-[[3-oxo-7-(3-phenyl-1-propynyl)-2(3H)-isoquinolinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



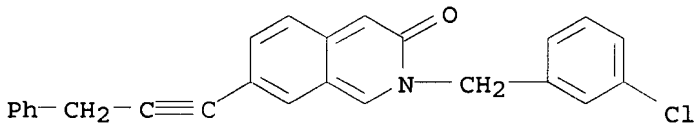
RN 662139-40-4 USPAT2
CN 3(2H)-Isoquinolinone, 2-[(4-fluorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



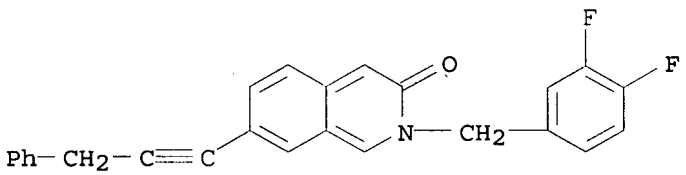
RN 662139-41-5 USPAT2
CN 3(2H)-Isoquinolinone, 7-(3-phenyl-1-propynyl)-2-[[3-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



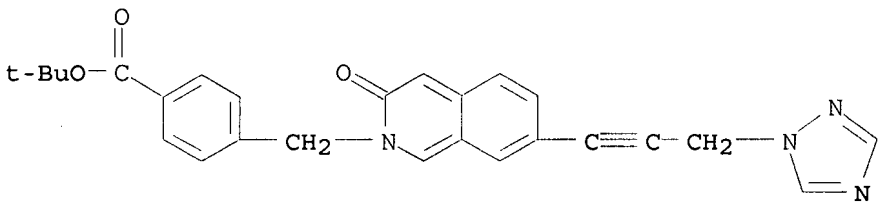
RN 662139-42-6 USPAT2
CN 3(2H)-Isoquinolinone, 2-[(3-chlorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



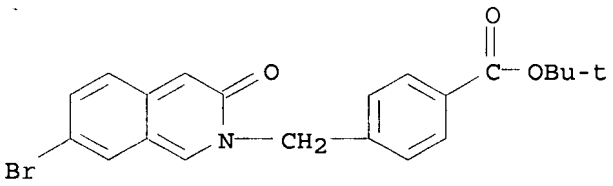
RN 662139-43-7 USPAT2
CN 3(2H)-Isoquinolinone, 2-[(3,4-difluorophenyl)methyl]-7-(3-phenyl-1-propynyl)- (9CI) (CA INDEX NAME)



RN 662139-44-8 USPAT2
CN Benzoic acid, 4-[[3-oxo-7-[3-(1H-1,2,4-triazol-1-yl)-1-propynyl]-2(3H)-isoquinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 662139-45-9P, 4-[(7-Bromo-3-oxo-2H-isoquinolin-2-yl)methyl]benzoic acid tert-butyl ester
(intermediate; preparation of isoquinolinone derivs. as selective MMP-13 inhibitors for use as antiarthritics)
RN 662139-45-9 USPAT2
CN Benzoic acid, 4-[(7-bromo-3-oxo-2(3H)-isoquinolinyl)methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)


O
C
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Br

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L5            3 S L4
L6            3 S L5 AND INFLAMMATION
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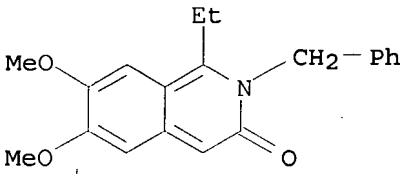
L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 309720-09-0 REGISTRY
ED Entered STN: 19 Dec 2000
CN 3(2H)-Isoquinolinone, 1-ethyl-6,7-dimethoxy-2-(phenylmethyl)- (CA INDEX NAME)
MF C20 H21 N O3
SR Chemical Library
Supplier: Zelinsky Institute of Organic Chemistry
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.30	34.00

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CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'TOXCENTER' ENTERED AT 11:07:16 ON 31 OCT 2007
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=> s l4
L5 3 L4

=> s l5 and inflammation
L6 3 L5 AND INFLAMMATION

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in at least one of the files. Refer to file specific help messages
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L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41337 CAPLUS
DOCUMENT NUMBER: 140:105253
TITLE: Compounds and methods for treating cancer and inflammation
INVENTOR(S): Zhang, Zaihui; Charest, David L.; Yan, Jun
PATENT ASSIGNEE(S): Kinetek Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004004834	A1	20040115	WO 2003-CA975		20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2491614	A1	20040115	CA 2003-2491614		20030625
AU 2003281245	A1	20040123	AU 2003-281245		20030625
US 2006148848	A1	20060706	US 2005-520250		20051028
PRIORITY APPLN. INFO.:			US 2002-393700P	P	20020702
			WO 2003-CA975	W	20030625

OTHER SOURCE(S): MARPAT 140:105253
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Compounds and methods for treating cancer and inflammation
AB Methods of using isoquinolone derivs. to treat cancer or inflammation in a mammal and pharmaceutical compns. containing such derivs. are disclosed.
ST antitumor SGK kinase inhibitor cancer inflammation therapy
IT Angiogenesis
Anti-inflammatory agents
Antitumor agents
Apoptosis
Human
Inflammation
Mammalia
Neoplasm
(compds. for treating cancer and inflammation)
IT Interleukin 6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compds. for treating cancer and inflammation)

IT Cell division
(reduction; compds. for treating cancer and inflammation)
IT 178037-70-2, Serum and glucocorticoid inducible kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2α; compds. for treating cancer and inflammation)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compds. for treating cancer and inflammation)
IT 23214-92-8, Doxorubicin 309720-09-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. for treating cancer and inflammation)

L6 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER:	2006:175398 USPATFULL			
TITLE:	Compounds and methods for treating cancer and inflammation			
INVENTOR(S):	Zhang, Zaihui, Vancouver, CANADA Charest, David L, Vancouver, CANADA Yan, Jun, Coquitlam, CANADA			
PATENT ASSIGNEE(S):	QLT, Inc. (non-U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006148848	A1	20060706	
APPLICATION INFO.:	US 2003-520250	A1	20030625	(10)
	WO 2003-CA975		20030625 20051028	PCT 371 date
	NUMBER		DATE	
PRIORITY INFORMATION:	US 2002-393700P		20020702 (60)	
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092, US			
NUMBER OF CLAIMS:	40			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1843			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Compounds and methods for treating cancer and inflammation

AB Methods of using isoquinolone derivatives to treat cancer or inflammation in a mammal and pharmaceutical compositions containing such derivatives are disclosed.

SUMM Uncontrolled signaling has been implicated in a variety of disease conditions including, inflammation, cancer, arteriosclerosis, and psoriasis. For example, many cancer causing genes (oncogenes) are protein kinases, enzymes that catalyze protein phosphorylation reactions,. . .

SUMM This invention is directed to the use of certain isoquinolone derivatives in treating hyperproliferative disorders, e.g., cancer, inflammation, etc. in a mammal. Of particular interest are hyperproliferative disorders associated with cellular modulation of protein phosphorylation states, i.e. altered. . .

SUMM In another aspect, this invention provides a pharmaceutical composition useful in treating cancer or inflammation in a human, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier, diluent or excipient and a compound of formula. . .

SUMM In another aspect of the invention, the use of the compounds of formula

(I) for the treatment of cancer, inflammation, or disorders or condition associated with hyperproliferation and tissue remodelling or repair is provided.

DETD . . . (I) which, when administered to a mammal, preferably a human, is sufficient to effect treatment, as defined below, for cancer, inflammation, or neurological disease. The amount of a compound of formula (I) which constitutes a "therapeutically effective amount" will vary depending. . .

DETD (i) preventing cancer or inflammation from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been. . .

DETD (ii) inhibiting cancer or inflammation, i.e., arresting its development; or

DETD (iii) relieving cancer or inflammation, i.e., causing regression of the condition.

DETD The compounds and pharmaceutical compositions of the invention are administered to a subject having a cancer or a pathological inflammation in order to inhibit tumour growth by impeding cell division, and to decrease inflammation by inhibiting cell adhesion and cell migration.

DETD . . . regrowth of tumours, prevent metastatic growth, diminish restenosis associated with cardiovascular surgery, to prevent or reduce cell migration leading to inflammation and associated tissue damage. Alternatively, the compounds and pharmaceutical compositions of the invention may be administered to a subject in. . .

DETD . . . invention. Other disorders and conditions of interest relate to epidermal hyperproliferation, tissue remodelling and repair. For example, the chronic skin inflammation of psoriasis is associated with hyperplastic epidermal keratinocytes.

DETD . . . treatment. The compounds and pharmaceutical compositions of the invention are administered to a subject having a cancer or a pathological inflammation in order to inhibit tumour growth by impeding cell division, and to decrease inflammation by inhibiting cell adhesion and cell migration. The compounds of formula (I) may also find use as affinity reagents for. . .

DETD . . . composition of the present invention may contain one or more known pharmacological agents used in the treatment of cancer or inflammation in a mammal, particularly, cancer or inflammation associated with hyperproliferation and tissue remodelling or repair.

DETD Of the various methods of treating cancer or inflammation in a mammal as set forth above in the Summary of the Invention, a preferred method is that method wherein the cancer or inflammation is associated with hyperproliferation or cell survival. Another preferred method is that method wherein the cancer or inflammation is associated with the activity SGK.

DETD . . . of the Invention, may not possess pharmacological activity as such, they may be administered to a mammal with cancer or inflammation and thereafter metabolized in the body to form compounds of the invention which are pharmacologically active. Such derivatives may therefore. . .

DETD A. Establishment of inflammation assay panel.

CLM What is claimed is:

1. A pharmaceutical composition useful in treating cancer, inflammation or a hyperproliferative disorder in a human, wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier, diluent or excipient and. . .

40. A method of treating cancer, inflammation or a hyperproliferative disorder in a mammal, which method comprises

administering to the mammal in need thereof a therapeutically effective.

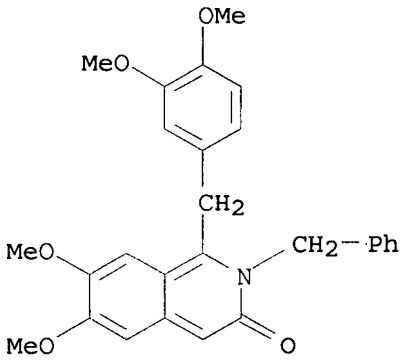
42. The method according to claim 40 wherein the cancer or inflammation is associated with hyperproliferation or cell survival.

43. The method according to claim 40 wherein the hyperproliferative disease, cancer or inflammation is associated with the activity of SGK.

IT 23214-92-8, Doxorubicin 309720-09-0
(compds. for treating cancer and inflammation)

L6 ANSWER 3 OF 3 TOXCENTER COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:30161 TOXCENTER
COPYRIGHT: Copyright 2007 ACS
DOCUMENT NUMBER: CA14008105253X
TITLE: Compounds and methods for treating cancer and inflammation
AUTHOR(S): Zhang, Zaihui; Charest, David L.; Yan, Jun
CORPORATE SOURCE: ASSIGNEE: Kinetek Pharmaceuticals, Inc.
PATENT INFORMATION: WO 2004004834 A1 15 Jan 2004
SOURCE: (2004) PCT Int. Appl., 66 pp.
CODEN: PIXXD2.
COUNTRY: CANADA
DOCUMENT TYPE: Patent
FILE SEGMENT: CAPLUS
OTHER SOURCE: CAPLUS 2004:41337
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Feb 2004
Last Updated on STN: 19 Sep 2006
TI Compounds and methods for treating cancer and inflammation
AB Methods of using isoquinolone derivs. to treat cancer or inflammation in a mammal and pharmaceutical compns. containing such derivs. are disclosed.
ST Miscellaneous Descriptors
antitumor SGK kinase inhibitor cancer inflammation therapy
RN 178037-70-2 (Serum and glucocorticoid inducible kinase)
10102-43-9 (Nitric oxide)
23214-92-8 (Doxorubicin)
RN 309720-09-0

L7 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:11444 CAPLUS <<LOGINID::20071031>>
DOCUMENT NUMBER: 78:11444
TITLE: 3(2H)-Isoquinolones. 1. 3-Oxygenated analogs of papaverine as peripheral vasodilators
AUTHOR(S): Kreighbaum, William E.; Kavanaugh, William F.; Comer, William T.; Deitchman, David
CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville, IN, USA
SOURCE: Journal of Medicinal Chemistry (1972), 15(11), 1131-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 41148-59-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cardiovascular activity of)
RN 41148-59-8 CAPLUS
CN 3(2H)-Isoquinolinone, 1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxy-2-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



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